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PATENT LEGAL DEPARTMENT/A-42-C
BECKMAN COULTER, INC.
4300 N. HARBOR BOULEVARD
BOX 3100
FULLERTON, CA 92834-3100

EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 06/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,308	REDDY ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,18,20-25,27,29 and 32-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,18,20-25,27,29 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S. 00.

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection (e.g., see 3/21/05 Response; the Examiner notes that Applicants' request to withdraw finality is moot in light of Applicants' filing an RCE i.e., see 3/21/05 Response, page 9, section I). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/21/05 has been entered. Claims 1-15, 18 and 20-36 were pending. Applicants amended claims 1, 12, 20, 27, 29 and 32-34. In addition, Applicants canceled claims 16-17, 19, 26, 28, 30-31 and 35-36. Therefore, claims 1-15, 18, 20-25, 27, 29 and 32-34 are pending and examined on the merits.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

Withdrawn Objections/Rejections

2. All previous rejections are withdrawn in view of Applicants' arguments and/or amendments.

New Rejections

Claims Rejections - 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 9-11, 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention. This is a new matter rejection.

Claim 1, from which claims 9-11 and 18 depend, was amended in the 3/21/05 Response. However, applicant did not show where support for these amendment(s) and/or addition(s) can be found in the specification. Specifically, the current amendment to claim 1 alters the scope of claims 9-11 and 18. For example, the use of a tertiary organic base no longer corresponds to the L_1-X-L_2 coupling step (i.e., it would appear that Applicants failed to update the method step in the corresponding dependent claim). Likewise, the use of an aqueous solution no longer corresponds to the step wherein the activated solid support is reacted with the biological molecule (i.e., it would appear that Applicants failed to update the method step in the corresponding dependent claim). Furthermore, the use of a washing step seems to be inapplicable to steps (a) and (c) (e.g., see 35 U.S.C. 112, second paragraph rejection below). If applicant believes this rejection is in error, applicant must disclose where in the specification support for this amendment can be found in accordance with MPEP 714.02. Therefore, claim 9-11 and all dependent claims represent new matter.

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For **claim 18**, the washing step is vague and indefinite when applied to steps (a) and (c) because there is nothing to wash away. For example, step (a) states, "providing a solid support comprised of an organic copolymer having at least one available amino group" (e.g., see newly amended claim 1; compare also to claim 21 wherein the washing step occurs after steps (b) and (d), not (a) and (c)). Thus, there are no "non-bound" compounds that can be washed away. Applicants are requested to clarify and/or correct. Therefore, claims 18 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-2, 9, 11, 18, 20, 21, 27 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Hammen (U.S. Patent No. 5,240,602) (Date of Patent is **August 31, 1993**).

For ***claims 1, 20, 27 and 33***, Hammen (see entire document) discloses methods for making chromatographic materials (e.g., see Hammen, abstract), which anticipates the claimed invention. For example, Hammen discloses **(a)** providing a solid support , comprised of an organic polymer having at least one available amino group (e.g., see column 21, Examples 22-23, especially lines 12-13, "To couple the PEG 600 to the amine derivatized resin"; see also line 16 wherein "polystyrene" is disclosed as the organic polymer; see also column 7, lines 30-36, "Solid supports which may be used in practicing the invention include ... various polymeric resins such as cross-linked polystyrenes"). Hammen also discloses **(b)** reacting the available amino group on the solid support with an activating compound, the activating compound having the structure: L_1-X-L_2 wherein L_1 and L_2 are leaving groups, and X is a moiety capable of nucleophilic substitution so that the reaction results in L_1 being displaced by the available amino group on the solid support to form an activated solid support (e.g., see column 21, lines 12-18, "To couple the PEG 600 to the amine derivatized resin, four equivalents of PEG 600 are activated by two moles of carbonyldiimidazole/mole PEG [i.e., which forms the activated PEG L_1-X-L_2 compound, Imidazole-(O=)C-O-PEG-O-C(=O)-Imidazole, that is subsequently reacted with the amine derivatized resin] ... this dioxane solution [containing the L_1-X-L2 compound] is then added to the amine derivatized polystyrene [i.e., solid support with amino group] to afford a urethane linked PEG with a carbonyl-diimidazole activated terminus [i.e., Imidazole-(O=)C-O-PEG-O-C(=O)-NH-Resin, wherein the "O-C(=O)-NH" portion represents the urethane]"). Hammen further discloses **(c-d)** providing a biological molecule having at least one reactive amino, thiol,

or hydroxyl group, the biological molecule being a macromolecule selected from the group consisting of nucleic acids, polypeptide chains, and carbohydrates and reacting the biological molecule with the activated support, thereby displacing the L_2 and covalently attaching the biological molecule to the solid support (e.g., see column 21, lines 23-27, "The CDI [carbonyl diimidazole] activated polystyrene is exposed to 1.0 mg of goat anti-human IgG [i.e., the macromolecule] ... to afford a polystyrene surface to which the human IgG is linked via PEG [i.e., the L2 was displaced to allow for the formation of a covalent bond between the IgG and the PEG"; see also Summary of the Invention).

For ***claim 2***, Hammen discloses "imidazole" rings (e.g., see Examples 22-23 wherein PEG 600 activated with CDI is disclosed).

For ***claim 9***, Hammen discloses pyridine and/or dioxane for step (a) and dioxane for step (b) (e.g., see column 21, Example 22).

For ***claim 11***, Hammen discloses 0.1 M aqueous sodium phosphate buffer (e.g., see Example 23).

For ***claims 18 and 21***, Hammen discloses a washing step (e.g., see column 21, lines 25-26, "Unreacted antibody is removed by rinsing [i.e., washing] three times with the same buffer").

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-4, 9-11, 18, 20, 21, 25, 27, 29 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hammen (U.S. Patent No. 5,240,602) (Date of Patent is **August 31, 1993**) and Hearn (Hearn, M. T. W. 1,1'-Carbonyldiimidazole-Mediated Immobilization of Enzymes and Affinity Ligands in "Methods in Enzymology" Ed. Mosbach, K. New York: Academic Press, Inc. **1987**, Vol. 135, pages 102-117) (of record) and Stolowitz et al. (WO 87/06586) (of record).

For ***claims 1-2, 9, 11, 18, 20, 21, 27 and 33***, Hammen teaches all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates and, as a result, renders obvious claims 1-2, 9, 11, 18, 20, 21, 27 and 33.

The prior art teaching of Hammen differ from the claimed invention as follows:

For ***claim 3***, Hammen differs from the claimed invention by not specifically reciting the use of an "X" selected from -C(=O)-, -S(=O)-, etc. (see Hammen, claim 3).

For ***claim 4***, Hammen differs from the claimed invention by not specifically reciting the use of 1,2,4-carbonyl di-triazole.

For ***claim 10***, Hammen differs from the claimed invention by not specifically reciting the use of tertiary organic base in step (a) (see also 35 U.S.C. § 112, second paragraph rejection above).

For ***claim 25***, Hammen differs from the claimed invention by not specifically reciting the use of a nucleic acid.

For ***claim 29***, Hammen differs from the claimed invention by not specifically reciting the use of a hormone, therapeutic drug, and/or drug of abuse.

However, the combined references of Hearn and Stolowitz et al. teach the following limitations that are deficient in Hammen:

For ***claim 3***, The combined references of Hearn and Stolowitz et al. (see entire document) teach, for example, -C(=O)- (e.g., see Hearn, abstract wherein CDI contains the requisite carbonyl; see also Stolowitz et al., abstract, "The invention relates to the functionalization of particulate bonded phase chromatographic supports prepared by silanization of silica gel or controlled pore glass and containing pendant primary alkyl amine groups. Functionalization results from the activation of the amines by reaction with N,N'-carbonyldiimidazole (CDI), or a related azolide, in anhydrous organic solvent, followed by derivatization of the support. Derivatization results from reaction of the activated support with a functionalizing reagent consisting of a primary or secondary, alkyl or aryl amine in organic solvent, or from an aqueous solution of the amine or its salt. A urea linkage results through which the functionalizing reagent is covalently

attached to the support"; see also page 9, formula 7 wherein the urea linkage is shown; see also Summary of Invention, "In addition, a number of important specific objectives are also achieved using the present invention, including: The use of N,N'-carbonyldiimidazole for the activation of a chromatographic support with other than pendant hydroxyl groups; The preparation of a urea derivative of a bonded phase chromatographic support and the unique hydrophilic nature of the urea linkage"; see also Example 1, lines 8-18; see also page 3, lines 14-20; see also page 3, lines 21-26).

For ***claim 4***, The combined references of Hearn and Stolowitz et al. disclose, for example, 1,2,4-carbonyl di-triazole (e.g., see Hearn, page 106, paragraph 1; see also page 107, Table I; see also Stolowitz et al., page 10, paragraph 1, "A variety of azolides other ... may be employed ... include[ing] N,N'-carbonyldipyrazole, N,N'-carbonyldi-1,2,3-triazole, N,N'-carbonyldi-1,2,4-triazole, N,N'-carbonyldiindole, N,N,-carbonylidibenzimidazole and N,N'-carbonyldibenztriazole and others").

For ***claim 10***, The combined references of Hearn and Stolowitz et al. disclose, for example, triethylamine (e.g., see Hearn, page 110, paragraph 1).

For ***claim 25***, The combined references of Hearn and Stolowitz et al. disclose polynucleotides (e.g., see Hearn, page 110, first full paragraph, "The reaction of N-nucleophiles ... such as ... amino acids, peptides, proteins and polynucleotides ... with CDI activated matrices").

For ***claim 29***, The combined references of Hearn and Stolowitz et al. disclose the use of biological molecules selected from the group consisting of hormones, therapeutic drugs and drugs of abuse as disclosed in claim 29 (e.g., see Hearn, page 112, Table IV).

It would have been obvious to one skilled in the art at the time the invention was made to immobilize affinity ligands for purposes of chromatographic separations as taught by Hammen using CDI in conjunction with "free amino groups" [e.g., by bonding the amino-derivatized resin directly to the ligand using CDI or derivatizing the PEG spacer with amino groups] as taught by the combined teachings of Hearn and Stolowitz et al. because Stolowitz et al. explicitly state that "free amino groups" can be used in conjunction with CDI for this purpose (e.g., see Stolowitz et al., abstract; see also Formulas I-IV; see also Hearn, Introduction; see especially reactions of pages 105-106). Thus, Hammen, Hearn and Stolowitz et al. represent analogous art because all three references teach the use of CDI for the immobilization of affinity ligands. Furthermore, one of ordinary skill in the art would have been motivated to use the "free amino groups" in conjunction with CDI as taught by the combined teachings of Stolowitz et al. and Hearn because Stolowitz et al. explicitly state that they obtain "near quantitative derivatization of bonded supports ... by this synthetic route" (e.g., see Stolowitz et al., page 4, lines 29-30). Stolowitz et al. also state that their method is "versatile" because "almost [an] infinite variety of ligands ... can be employed as functionalizing reagents" (e.g., see Stolowitz et al., page 4, lines 34-35) and their method allows for "[t]he use of N,N'-carbonyldiimidazole for the activation of a chromatographic support with other than pendant hydroxyl groups" (e.g., see Stolowitz et al., page 4, lines 23-25). In addition, Stolowitz et al. state that their method provides for a physical barrier that enhances the efficiency of the chromatographic procedures (e.g., see Stolowitz et al., page 4, lines 11-19, "The preparation of a physical barrier preventing interaction between surface silanols

and sample components; The derivatization of the physical barrier preventing interaction between the hydrophobic silane backbone and sample components; and the functionalization of the physical barrier to impart properties resulting in selective retention of sample components", which augments the teachings of Hammen that was drawn to the use of PEG spacer molecules to prevent non-specific binding. Stolowitz et al. also state that the "urea" linkage has favorable properties (e.g., see Stolowitz et al., page, 7, first full paragraph, "The urea linkage ... is uncharged under normal chromatographic conditions and provides a hydrophilic barrier masking the properties of the silane backbone and the residual silanol activity beneath it"). Hearn also teaches that CDI can be used to obtain chromatographic separations with "very high purification" using "polynucleotide" ligands (e.g., see Hearn, page 102, Introduction). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because both Hammen, Hearn and Stolowitz et al. use the same coupling reagents (e.g., CDI) with the same solid supports (e.g., see Hammen, page 109, paragraph 1 wherein porous silicas, controlled pore glasses are disclosed; see also Stolowitz et al., "Summary of Invention" wherein controlled pore glasses and porous silicas are also disclosed). Stolowitz et al. also state, "almost [an] infinite variety of ligands ... can be employed as functionalizing reagents" (e.g., see Stolowitz et al., page 4, lines 34-35), which would include the "larger" peptide/protein "macromolecules" disclosed by Hammen and the nucleic acid ligands of Hearn.

9. Claims 1-15, 18, 20-25, 27, 29 and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hammen (U.S. Patent No. 5,240,602) (Date of Patent is **August 31, 1993**) and

Hearn (Hearn, M. T. W. 1,1'-Carbonyldiimidazole-Mediated Immobilization of Enzymes and Affinity Ligands in "Methods in Enzymology" Ed. Mosbach, K. New York: Academic Press, Inc. **1987**, Vol. 135, pages 102-117) (of record) and Stolowitz et al. (WO 87/06586) (of record) and Milton (US 6,146,833) (of record) and Okamoto et al. (US 6,476,215) (of record) and Guo et al. (Nuc. Acids Res. 1994, pp. 5456-5465) (of record).

For ***claims 1-4, 9-11, 18, 20, 21, 25, 27, 29 and 33***, the combined teachings of Hammen, Hearn and Stolowitz et al. disclose all the limitations stated in the 35 U.S.C. 103(a) rejection above (incorporated in its entirety herein by reference), which renders obvious claims 1-4, 9-11, 18, 20, 21, 25, 27, 29 and 33.

The prior art combined teachings of Hammen, Hearn and Stolowitz et al. differ from the claimed invention as follows:

For ***claims 5-6, 22-23***, the prior art teachings of Hammen, Hearn and Stolowitz et al. differ from the claimed invention by not reciting the deposition of compounds in a particular area on the support (e.g., using inkjet printing).

For ***claims 7-8, 24***, the prior art teachings of Hammen, Hearn and Stolowitz et al. differ from the claimed invention by not reciting the use of a humid chamber.

For ***claims 12-15 and 32***, the prior art combined teachings of Hammen, Hearn and Stolowitz et al. differ from the claimed invention by not reciting the use of a plate or film.

For ***claim 34***, the prior art combined teachings of Hammen, Hearn and Stolowitz et al. differ from the claimed invention by not reciting the use of an amino derivatized oligonucleotide. Hammen, Hearn and Stolowitz et al. state that

oligonucleotides can be used, but not state that such oligonucleotides are amino derivatized.

However, the combined references of Milton et al. Okamoto et al. and Guo et al. teach the following limitations that are deficient in the combined teachings of Hammen, Hearn and Stolowitz et al.:

For ***claims 5-6, 22-23***, However, the use of printing techniques to deposit biological compounds onto solid supports was well established in the art at the time of filing, as evidenced by the references of Milton, Okamoto et al. and Guo et al. (e.g., see for example, column 12, lines 24-41; see also column 8, line 33; see also column 11, line 62; see also column 17, line 2; see also Guo et al., page 5457, 1st column; see also Okamoto et al., columns 1-3). The reference teaches methods for printing compounds to make an array. See Examples 5 and 6 wherein spot diameter is, for example, 250 μm (note this procedure is *referred to in the instant specification,* pages 9 and 10). Milton specifically teaches the immobilization of e.g. oligonucleotides and peptides, see Examples 3-9 of the reference.

For ***claims 7-8 and 24***, the combined references of Milton, Okamoto et al. and Guo et al further teach a humid chamber during the attachment of the probes to their arrays (e.g., see Guo, page 5457, 1st column; see also Okamoto et al., column 18, lines 42-46). This step is used to complete the reaction and/or to incubate the arrays.

For ***claims 12-15, 32***, the combined references of Milton, Okamoto et al. and Guo et al. further teach the use of a plate and a film (e.g., see figures 1-7; see also column 2, lines 5-8 wherein glass slides, polymer films, silicon wafers are disclosed; see also column 2, lines 47-50; see also column 3, line 4; see especially claim 23, "the solid

support provided is a film"). In addition, Milton teaches polypropylene, which is an organic polymer (e.g., see column 2, line 5; see also figures 1, 6, 10, 14; see also Examples; see also claims 2, 4, 8 and 11).

For ***claim 34***, the combined references of Milton, Okamoto et al. and Guo et al. further teach the use of amino derivatized oligonucleotides (e.g., see .

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the carbonyl diimidazole (CDI) immobilization chemistry as taught by Hammen, Hearn and Stolowitz et al. in an array-type format using a "printing method" to deliver the amine compound (e.g. oligonucleotides or peptides) as taught by Milton, Guo and Okamoto because "immobilization" of biomolecules is required in each case (i.e., the references represent analogous art). One of ordinary skill would have been motivated to do so due in order to create covalently attached amine bound biomolecules "immobilized at site specific locations" as taught by Milton (for example). In addition, a person of skill in the art would have been motivated to use a "humid chamber" to complete the reaction and/or to incubate the arrays once created.

In addition, it would have been obvious to one skilled in the art at the time the invention was made to immobilize affinity ligands in an array format for analytical and diagnostic purposes as taught by the combined references of Milton, Okamoto et al. and Guo et al. (e.g., see Milton et al., abstract) using the CDI immobilization procedures as taught by the combined teachings of Hammen, Hearn and Stolowitz et al. because Stolowitz et al., for example, explicitly state that CDI can be used for this purpose (e.g., see Stolowitz, column 6, lines 43-56, "An 'affinity ligand' ... may also be used as a

diagnostic reagent ... [which] permits the detection and/or quantitation of such biological molecules"; see also lines 23-26, "'the chromatographic material containing the affinity ligand may comprise ... the inner surface of a microtitre plate [i.e., an array]"). Furthermore, one of ordinary skill in the art would have been motivated to use the CDI immobilization techniques as taught by the combined teachings of Hammen, Hearn and Stolowitz et al. because Stolowitz et al., for example, explicitly state that they obtain "near quantitative derivatization of bonded supports ... by this synthetic route" (e.g., see Stolowitz et al., page 4, lines 29-30). Stolowitz et al. also state that their method is "versatile" because "almost [an] infinite variety of ligands ... can be employed as functionalizing reagents" (e.g., see Stolowitz et al., page 4, lines 34-35). In addition, the combined references of Hammen, Hearn and Stolowitz et al. state that their method provides for a physical barrier that decreases non-specific binding that might otherwise interfere with an analytical and/or diagnostic assay (e.g., see Hammen, column 2, lines 56-58, "Accordingly, it is an object of the present invention to provide chromatographic material which is substantially free of reversible non-specific adsorption"; see also Stolowitz et al., page 4, lines 11-19, "The preparation of a physical barrier preventing interaction between surface silanols and sample components; The derivatization of the physical barrier preventing interaction between the hydrophobic silane backbone and sample components; and the functionalization of the physical barrier to impart properties resulting in selective retention of sample components"; see also page 7, first full paragraph, "The urea linkage ... is uncharged under normal chromatographic conditions and provides a hydrophilic barrier masking the properties of the silane backbone and the

residual silanol activity beneath it"), which the combined teachings of Milton, Okamoto et al. and Guo et al. recognize as being "crucial" for the proper operation of their diagnostic arrays (e.g., see Milton, column 6, lines 38-43, "This [non-specific binding] is an important consideration because diagnostic applications which depend upon detecting reagents specifically bound to biopolymers immobilized to solid supports cannot tolerate nonspecific binding to the solid support").

Finally, one of ordinary skill in the art would have reasonably expected to be successful because Stolowitz et al. also state, "almost [an] infinite variety of ligands ... can be employed as functionalizing reagents" and Hammen provide a specific example of a protein, which would encompass the proteins disclosed by Milton (e.g., see Stolowitz et al., page 4, lines 34-35; see also Hammen, figure 3-6 and 10, disclosing various proteins; compare to Milton, column 11, lines 28-30, "Similarly any protein or peptide with surface amino groups, e.g. lysine can be immobilized to a solid support"). In addition, both Hammen and Milton disclose the use of compatible polymeric materials such as polyvinyl alcohol (e.g., see Milton, column 6, paragraph 2, "... polymeric materials capable of being derivatized ... include a wide range of materials ... polyvinyl alcohol"; see also Hammen, definitions section, "A 'substantially non-ionic hydrophilic spacer' is ... polyvinyl alcohol"). In addition, all references teach the use of CDI for immobilization (e.g., compare Hammen, Examples wherein CDI is disclosed to Milton, column 8, lines 37-55, "In another aspect, the present invention provides methods for preparing reagents for immobilizing biopolymers which include providing a solid support fabricated of ethylene acrylic acid copolymer or ethylene methacrylic acid copolymer and

derivatizing at least one surface of the solid support by reacting the surface with an activating agent. Suitable activating agents are ... carbodiimides"; see also Example 9 wherein the use of diisopropylcarbodiimide is disclosed) (emphasis added). Finally, both Hammen and Milton disclose that protein immobilization can be used for the same diagnostic and/or analytical purpose (see above).

Response

10. To the extent that Applicants' arguments against the previous 35 U.S.C. § 103(a) rejections can be applied to the new 35 U.S.C. § 103(a) rejections above, the following arguments are made of record.

[1] Applicants argue, "Hearn does not teach Applicants' claimed 'organic polymer having at least one available amino group' ... [and] Stolowitz et al., Okamoto et al., and Guo et al. ... do not remedy the deficiencies of Hearn" (e.g., see 3/21/05 response, page 11, middle paragraph).

[2] Applicants argue, "one of ordinary skill in the art would not be motivated to modify or combine Hearn and Milton because the proposed combinations of Milton and Hearn changes the principle of operation of the references and the proposed combination would not result in an "immobilization" of biomolecules" and cite MPEP § 2143.01 in support of this contention (e.g., see 3/21/05 Response, page 12, paragraph 1).

[3] Applicants argue, "Milton teaches immobilizing biopolymers on solid supports having acyl fluoride functionalities ... The acyl fluoride functionality is then reacted with an amino derivatized biopolymer ... Reacting an acyl fluoride with the CDI described in Hearn

would not result in attachment of the CDI ... Accordingly, the modification changes the principle of operation" (e.g., see 3/21/05 Response, page 12, last two paragraphs).

[4] Applicants argue that Milton provides only a "teaching away" from an organic polymer having at least one available amino group (e.g., see 3/21/05 Response, page 13).

This is not found persuasive for the following reasons:

[1] The Examiner contends, for example, that Hammen teaches organic polymers having at least one available amino group (e.g., see 35 U.S.C. § 102 rejection above) and, as a result, there is no deficiency.

[2] The Examiner contends that no such change in principle of operation exists. Both references are drawn to the immobilization of biomolecules use carbodiimides (see new 103 rejection above) and thus MPEP § 2143.01 is not applicable.

[3-4] The Examiner respectfully disagrees. Applicants have failed to appreciate the full teachings of the Milton reference. In contrast to Applicants' assertions, the Examiner contends that Milton explicitly discloses the use of carbodiimides (e.g., see Milton, column 8, lines 37-55, "In another aspect, the present invention provides methods for preparing reagents for immobilizing biopolymers which include providing a solid support fabricated of ethylene acrylic acid copolymer or ethylene methacrylic acid copolymer and derivatizing at least one surface of the solid support by reacting the surface with an activating agent. Suitable activating agents are ... carbodiimides"; see also Example 9 wherein the use of diisopropylcarbodiimide is disclosed as a preferred embodiment) (emphasis added). Furthermore, even if assuming arguendo Milton only discloses acyl fluoride functionality that would not preclude the combination of the references. The strongest rationale for combining references is a recognition, expressly or

impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Here, the beneficial result of the combination of references is, for example, a facile synthesis, quantitative immobilization and/or less non-specific binding. The Examiner also notes that non-preferred embodiments constitute prior art (e.g., see MPEP § 2123, "A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including non-preferred embodiments. Merck & Co. v. Biocraft Laboratories, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989)").

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
May 29, 2005

BENNETT CELSA
PRIMARY EXAMINER